Final Report

Title: Deep Space Flight Radiation Risk Assessment/Protection

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This report covering work performed at Fred Hutchinson Cancer Research Center on a grant administered by the Johnson Space Center represents the remainder of the work completed in the first year of a two-year study. The first portion of the work has already been reported in the "Final Report on Contract T8498S," an Interagency Agreement with the Lawrence Berkeley Laboratory. The second year of the grant is presently ongoing and is being administered out of NASA Headquarters, Washington, D.C., and will not be reported on here.

I. The *Additivity Assumption* in radiation risk assessment

The importance of testing the *additivity assumption* which is inherent in the present radiation risk assessment methodology has been studied. This assumption states that risks from individual components of a complex radiation field involving many different types of radiation can be added to yield the total risk of the complex radiation field. However, when the exposure is protracted over many cell doubling times (as will be the case for extended missions to the moon or Mars), the possibility exists that radiation effects that depend on multiple cellular events over a long time period, such as is probably the case in radiation-induced carcinogenesis, may not be additive in the above sense and the *exposure interval* may have to be included in the evaluation procedure. This problem is particularly important in the area of space radiation risk evaluation because of the many different types of high- and low-LET radiation present in the galactic cosmic ray environment.

Conclusions of the analysis are first that the "sensitive-window" hypothesis (formulated by Rossi, Kellerer, Brenner, Hall and Elkind) will not modify significantly the risk of tumor induction from the galactic cosmic radiation. Secondly, the exposure interval could play a pivotal role in determining the ultimate probability of tumor. If the two-stage stochastic model is a reasonable approximation of the carcinogenic process, as indicated by the good fits to data sets of radon-inhaling rats and a re-analysis of the Colorado Plateau miners and British physicians (studies performed by Moolgavkar and his assossiates), the length of exposure plays a critical role in

determining the probability of tumor-induction at least from the high-LET radiation contributions. This would imply that the modifying factor, Q, to be applied to the absorbed dose should be a function of exposure time as well as LET. Thus, the additivity assumption would break down, and a simple addition of risks over the entire spectrum of particles for long exposure times would be inappropriate. Further animal studies with appropriately designed experiments at high- and low-LET and for short and long exposure times are necessary to determine the magnitude of any such breakdown in the additivity assumption. Appropriately chosen epidemiological data sets might also be able to detect such a breakdown. Finally, the issue is an important one in low-LET radiation risk assessment, as the value of the appropriate DDREF (dose and dose-rate effectiveness factor) used to modify the high-dose-rate risk coefficients from the A-bomb survivors might turn out to depend strongly on the length of the exposure time being considered.

This work was presented as an invited paper at the 30th COSPAR meeting held in Hamburg, Germany, July 11-21 1994. It is presently in press in *Advances in Space Research.*

II. Reanalysis of the radon-inhaling rats from the Battelle study with the addition of cell killing

A reanalysis of the data on lung-tumor induction by radon-inhaling rats in the Battelle rat-lung carcinogenesis study, with the explicit inclusion of cell-killing within a two-stage model, shows that in this model it is probably the ore-dust carrying the radon that provides the promotion (enhanced net cell growth rate) of the initiated cell population. This promotion leads naturally to an "inverse dose-rate" effect for the probability of tumor; that is, for a given total exposure, higher probability of tumor for longer exposure time (lower dose-rate) than for shorter exposure time (higher dose-rate). Another conclusion of this study is that cell killing in the intermediate cell population cannot be neglected, at least from the high-LET component of a radiation environment. This work has lead to a paper that has been submitted to *Radiation Research.*

The following three publications have resulted from this research:

S. B. Curtis. Importance of dose-rate and cell proliferation in the evaluation of biological experimental results, *Adv. Space Res. 14* , (10)989-(10)996 (1994).

S. B. Curtis. Possible effects of protracted exposure on the additivity of risks from space radiations, *Adv. Space Res.*, in press.

E. G. Luebeck, S. B. Curtis, F. T. Cross and S. H. Moolgavkar. Two-stage model of radon-induced malignant lung tumors in rats: Effects of cell-killing, *Radiat. Res.* (submitted).